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Second External Review Draft

Research Needed To Improve Health and Ecological Risk Assessments for Ozone

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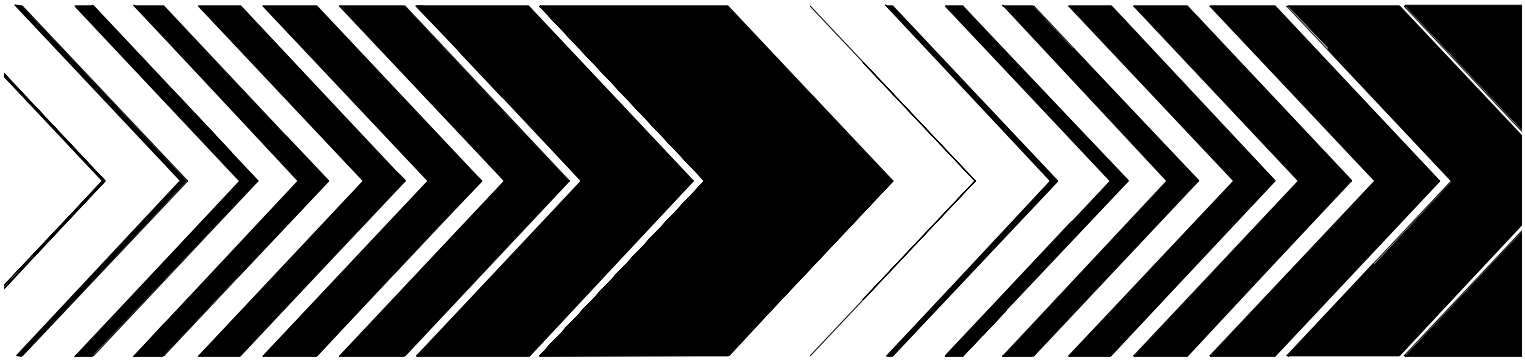

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RESEARCH NEEDED TO IMPROVE HEALTH AND ECOLOGICAL RISK ASSESSMENTS FOR OZONE

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CHAPTER 1. INTRODUCTION

Ozone is one of six criteria air pollutants whose ambient concentrations are regulated under the National Ambient Air Quality Standards (NAAQS) established by the U.S. Clean Air Act (U.S. Code, 1991). The NAAQS apply to both human health (primary standard) and public welfare (secondary standard). The Clean Air Act (Section 109) requires the Administrator of the Environmental Protection Agency (EPA) to set primary standards to protect sensitive members of the population from adverse health effects of criteria air pollutants, with an adequate margin of safety. The Clean Air Act (CAA) also states that "Any national secondary ambient air quality standard, as defined under Section 109(b)2, must specify a level of air quality the attainment and maintenance of which in the judgement of the Administrator, based on such criteria, is requisite to protect the public welfare from any known or anticipated adverse effects associated with the presence of such air pollutant in the ambient air." Welfare effects, as defined in §7602(2) of the U.S. Code (1999), include but are not limited to "effects on soils, water, crops, vegetation, manmade materials, animals, wildlife, weather, visibility, and climate, damage to and deterioration of property, and hazards to transportation, as well as effects on economic values and personal comfort and well-being."

The U.S. Environmental Protection Agency (EPA) document *Air Quality Criteria for Ozone and Related Photochemical Oxidants* (Ozone AQCD) published July 1996, comprehensively assembled, summarized, and interpreted available scientific evidence on exposure to, and health and ecological effects of, ambient ozone (O_3). Subsequent studies have provided important additional observations. There is clear agreement that short-term ozone exposure produces or promotes significant health effects, not merely temporary physiologic changes. Also, current experimental and epidemiologic evidence provides ample reason for suspicion that long-term ambient ozone exposure induces deleterious human health effects. At the same time, important uncertainties remain in the available health effects database for ambient ozone. This combination of legitimate concern and scientific uncertainty creates a strong case for continued health-related research on ozone, both alone and in combination with other environmental substances (e.g. air pollutants and aeroallergens). Chapter 2 summarizes

scientific evidence, and important remaining uncertainties, regarding the health effects of ozone exposure.

Chapter 3 summarizes scientific information and important uncertainties regarding ozone effects on agricultural crops, forests, and natural ecosystems. The effects of ozone on plants is both cumulative and long-term. Tropospheric ozone is pervasive and is considered to be the most important phytotoxic air pollutant worldwide. Basic changes in plant chemistry and yield reductions are due to the cumulative impact of ozone over a single growing season in the case of annuals and over multiple growing seasons in the case of perennial vegetation such as trees. In 1996, based on the Ozone AQCD and the accompanying EPA staff paper that analyzed and summarized the policy-relevant scientific and technical information in the AQCD, EPA proposed to revise the primary (health-based) and secondary (welfare-based) NAAQS for ozone. The secondary proposal included two separate alternatives for consideration, and public comment was solicited on both. One alternative was to make the secondary standard equal in form and level to the proposed new primary standard; the other was to set a separate secondary standard with a seasonal, cumulative form.

To help interpret existing information and identify remaining uncertainties and data gaps in the assessment of the effects of ozone on crops, forest and ecosystems, EPA gave priority to re-evaluation of the results of past ozone research efforts in a workshop held January 12-13, 1996, in cooperation with Southern Oxidant Study (SOS) investigators at North Carolina State University, Raleigh, NC. Scientists from throughout the United States and Canada, who had been studying the effects of ozone on crops, forests, and natural ecosystems were invited to discuss the state of scientific knowledge. The deliberations of this group produced a consensus on what was understood about the nature of ozone and its effects on plants and the appropriate index to be used to regulate ozone exposure. The consensus statement from the workshop stated: "There is a need for a secondary standard different from any of the primary standards being recommended by OAQPS [Office of Air Quality Planning and Standards]. Plants are more sensitive than humans and thus require a more restrictive standard. The effects of ozone on plants is both cumulative and long-term. Yield [effects] and basic changes in plant chemistry are due to the cumulative impact of ozone over a single growing season in the case of annuals and over multiple growing seasons in the case of perennial vegetation such as trees. For these

reasons, a Secondary Standard should be both cumulative and long-term." This consensus statement was submitted during the ozone standard review process.

However, although the Clean Air Scientific Advisory Committee (CASAC) of EPA's Science Advisory Board (SAB) and other parties concluded that there was a need to revise the 1-h secondary standard, CASAC also noted that there were too many uncertainties in the current scientific knowledge base to establish a secondary ozone NAAQS different from the primary standard. The EPA Administrator, therefore, decided to promulgate a secondary ozone NAAQS equal to the primary standard (0.08-ppm, 8-h). It was evident that high priority should be assigned to (a) identifying and reducing uncertainties relevant to the ozone standard setting process, and (b) to the conduct of additional research to provide improved bases for future decision making on secondary standards to better protect against ecological effects of ozone.

1.1 OZONE RESEARCH NEEDS WORKSHOPS

In accord with the above, EPA's National Center for Environmental Assessment, Research Triangle Park Division (NCEA-RTP) convened two workshops in early 1997 to elicit views from EPA and non-EPA experts with regard to the most important research issues needing to be addressed to reduce key uncertainties affecting ozone NAAQS development.

1.1.1 Health Research Needs Workshop, March 1997

In March 1997, a three-day scientific workshop, organized by NCEA-RTP, was held in Chapel Hill, NC, to identify research needed to reduce uncertainty in ozone health risk assessment and to identify future ozone health research directions. Workshop participants included health researchers, exposure assessment experts, and atmospheric scientists from inside and outside EPA (See Appendix I A for list of Workshop Participants). Workshop discussions identified and prioritized research needs in four disciplinary areas: (1) exposure assessment, (2) controlled exposure studies, (3) dosimetry and interspecies extrapolation, and (4) epidemiology and biostatistics. After the workshop, participants prepared written reports of their opinions as to the major outstanding ozone health research needs. The workshop and participants' reports served three valuable purposes: (1) to re-focus scientific attention on health

effects of ozone; (2) to emphasize that, although much has been learned regarding ozone health effects, there remain major gaps in the existing scientific database; and (3) to provide guidance toward articulating and prioritizing research needs as delineated in the present document.

1.1.2 Ecological Research Needs Workshop, May 1997

To identify and prioritize new research needed to improve future bases for EPA regulatory decisions regarding the secondary Ozone NAAQS, a workshop was held in Raleigh in May 1997. Representatives from EPA's National Environmental Research Laboratory (NERL), Office of Air Quality Planning and Standards (OAQPS), and NCEA-RTP worked together with SOS staff to develop the format for the workshop. A steering committee composed of scientists with extensive research experience in studying ozone effects on agricultural crops and ecosystems provided guidance on all aspects of the workshop. It was decided that both science and policy issues should be addressed by workshop participants. Scientists from academia and the public and private sectors were invited based on their expertise in several research areas (e.g., agricultural crops/forests/natural ecosystems; modeling/scaling; monitoring/meteorology; statistics; economics; risk assessment; and policy development). Representatives from various other Federal agencies (e.g. USDA, and Dept of Interior units) with interests and policy responsibilities regarding effects of air quality on ecological systems were also invited. The participants were from the United States, Canada, and Europe (See Appendix II A for list of Workshop Participants).

To place the workshop in a proper context, the introductory session provided an overview of the NAAQS review process, discussed scientific and regulatory policy needs, and the EPA ecological risk assessment paradigm. The participants were charged with considering these introductory points and with identifying important areas of scientific knowledge in which a great deal of uncertainty or notable information deficiencies exist. Each workshop session produced recommendations for research needed in the session topic area. These recommendations form an important basis of the ecological research needs for ozone presented in this document.

An ecological risk assessment process has been developed by EPA to assist in evaluating the likelihood that adverse ecological effects may occur or are occurring as a result of exposure to one or more stressors (U.S. EPA, 1992) These assessments are conducted to bring scientific information to bear on risk management decisions (e.g., Do current air standards afford sufficient

protection to ecological resources? What changes are needed to restore a valued ecosystem?). Research conducted to address needs identified in this document will serve as inputs to future risk assessments being developed to characterize ozone effects on ecosystems.

1.1.3 Ecological Research: Other Federal Agencies

It is evident that EPA will not be able to address all of the varied research needs presented in this document. It is anticipated that other agencies and research organizations will also use these recommendations, which emerged from the thoughtful workshop discussions among many experienced scientists and administrators, to identify research that fits into their environmental missions, either independently or cooperatively with other agencies (including EPA).

The U.S. Department of Agriculture (USDA) plays an important role in the stewardship of the nation's land and natural resources. The USDA's Agricultural Research Service (ARS); Forest Service (USFS); and Cooperative State Research, Education, and Extension Service (CSREES) also have as part of their missions the protection of our ecological resources. As the intramural research arm of USDA, part of the ARS mission is to maintain a quality environment and natural resource base. Forest Service research in the area of atmospheric sciences is intended to ensure that critical knowledge about atmospheric processes needed to understand air pollution effects important to forest management is available for managers, scientists, and the public.

The U.S. Department of the Interior (DOI) mission is, in part, to encourage and provide for the appropriate management, preservation, and operation of the nation's public lands and natural resources for use and enjoyment both now and in the future, and to carry out scientific research and investigations in support of these objectives. Within DOI, the U.S. Fish and Wildlife Service's mission is to conserve, protect, and enhance the habitats of fish and wildlife; part of their responsibility is the protection of wetlands. The National Park Service (NPS) mission is to promote and regulate the use of the national parks for the purpose of conserving their scenery and wildlife for the enjoyment of future generations. As part of this mission, the NPS assists other agencies in their research efforts in areas critical to protection of the national parks.

Several other agencies and organizations at both national and state levels, including the Tennessee Valley Authority, the National Council for Air and Stream Improvement, and the Electric Power Research Institute, have an interest and responsibility to protect our country's natural resources, including crop, forest, and natural ecosystems. It is likely that ambient ozone

is relevant to the research objectives of all of these agencies. Thus, they all have an interest in advancing understanding of the effects of ozone as a plant and ecosystem stressor.

1.2 OZONE RESEARCH AND THE CLEAN AIR SCIENTIFIC ADVISORY COMMITTEE (CASAC)

In November 1995, CASAC wrote the EPA Administrator a letter of closure on the portion of the ozone Staff Paper that addressed primary standards. An excerpt from that letter is presented below:

> "Since the last ozone . . . review, the scientific community has made great strides in their understanding of the health effects of ozone exposure because of ongoing research programs. . . . Nevertheless, there are still many gaps in our knowledge and large uncertainties in many of the [risk] assessments. For example, there is little information available on the frequency of human activity patterns involving outdoor physical exercise. Little is also known about the possible chronic health impacts of ozone exposure over a period of many years. In addition, there is no clear understanding of the significance of the inflammatory response inferred from the broncholavage data. Panel members stated, however, that the scientific community is now in a position to frame the questions that need to be better resolved so the uncertainties can be reduced . . . . For this reason, it is important that research efforts on the health and ecological effects of ozone not be reduced because we have come to closure on this review."

This excerpt highlights major areas of uncertainty in the health-related scientific database for ozone. It also underscores that, though some changes from past research priorities are in order, the overall need for continued ozone research has not diminished. Also, such research, if thoughtfully designed and adequately supported, can yield important advances in the understanding of ozone effects in the foreseeable future.

The present document is a second external review draft. The first external review draft was presented to CASAC in November 1998. CASAC's response was contained in a letter, dated January 29, 1999, to the EPA Administrator. In that letter, CASAC commented on weaknesses

in the first draft's content and organization, and made several recommendations for how to address the subject weaknesses. This second draft incorporates revisions made in response to the CASAC comments and recommendations.

The CASAC letter of January 29, 1999, also contained the following excerpt regarding ozone research in general:

> "The [CASAC] Panel would like to express an overriding concern that it considers more important than comments pertaining specifically to the [first external review] draft document. It was the consensus of the Panel that the Agency should develop and sustain a substantive, well-prioritized and integrated program of research on the health and welfare effects of ozone. The present level of research and the likely funding portrayed by EPA staff falls far short of an adequate effort…The Panel also noted the likely importance of co-pollutant effects, and encourages greater integration of research strategies for ozone, particulate matter, and other air contaminants."

The two CASAC excerpts presented above underscore the importance of revitalizing EPA's commitment to research on the health and ecological effects of ambient ozone exposure. The second excerpt also underscores the importance of studying ozone not only as a single pollutant, but also as a component of the complex ambient air pollution mix. As CASAC recognized in 1999, future research programs should treat multiple pollutants in a more even-handed fashion, in order to achieve full understanding of ambient air pollution health effects. Such even-handed treatment will also be useful in efforts to ascertain the health and ecological benefits of pollution control strategies targeted to single pollutants (e.g., selective reduction of individual NAAQS pollutants), relative to the benefits of multi-pollutant control strategies (e.g., control of sources responsible for multiple pollutants).

1.3 GOALS AND SCOPE OF THIS DOCUMENT

As discussed above, the available scientific database assessed in the 1996 Ozone AQCD was limited with regard to supporting precise quantitative health risk assessment for ozone, especially with regard to long-term exposure. Much further research is required to enhance this data base. One major goal of this document is to substantiate this point, and to direct (or re-

direct) attention of researchers and sponsoring organizations to this requirement. Toward this goal, the document delineates and prioritizes specific research needs to reduce uncertainty in ozone health risk assessment.

Another major goal is to promote cooperation among exposure assessment experts, epidemiologists, biostatisticians, and experimental health researchers in future ozone research. In the U.S. and other developed countries, ambient air pollution effects tend to be subtle in relation to effects of other risk factors, such as smoking and respiratory infection. Also, the etiology of air pollution-associated health disorders is multifactorial. Indeed, no known clinical disorder is specific to exposure to criteria air pollutants at current ambient U.S. levels. Thus, epidemiologic studies of ambient air pollution effects are inherently subject to some uncertainty, even when carefully designed and conducted. Also, thorough epidemiologic studies may effectively ascertain population-based exposure-response relationships, but epidemiologic studies can only rarely ascertain dose-response relationships. Therefore, experimental corroboration of epidemiologic findings, and quantitative extrapolation of experimental findings to the community situation, are also needed. Often, such corroboration requires experimental elucidation of relevant biological mechanisms. At the same time, epidemiologic research is needed to characterize the public health burden of air pollution exposure, to verify the relevance of experimental findings to public health, and to characterize the public health benefits of environmental regulation. Thus, further understanding of ozone's human health effects will be most effectively achieved by cooperation among scientific disciplines.

This document underscores the critical need for expansion of multi-pollutant health research. In this regard, the document addresses several general research areas in which joint assessment of ozone and other environmental agents, such as airborne particulate matter (PM), will advance understanding of the health effects of both. Hopefully, this will provide preliminary direction toward multi-pollutant health assessment. Detailed consideration of multi-pollutant research is beyond the scope of this document. Even so, the authors emphasize that such detailed consideration is urgently required. This effort should be initiated promptly, should encompass both research and regulatory issues, and should involve researchers, research-sponsoring organizations, and environmental risk managers.

The overall objective of future research on the effects of ozone on agricultural crops, natural and plantation forests and native vegetation components of ecosystems is to reduce

current uncertainties in determining exposure-response relationships under ambient conditions. A review of the OAQPS Staff Paper (EPA-452/R-96-007, June 1996) indicates that existing scientific uncertainties in a number of areas increased the uncertainties associated with characterizing qualitative and/or quantifiable risks to various components of agronomic, forested and natural ecosystems. These uncertainties made difficult selection of a secondary standard that would protect crops, forests, natural vegetation and ecosystems. Areas where additional information is needed include those below.

- **Exposure Dynamics:** monitoring to determine ambient ozone concentrations encountered in urban, rural farm/forest areas, exposure patterns (episodes), concentrations vs flux, relationship between chamber and field exposure data, plant uptake.
- **Plant Response/Mode of Action:** biological, chemical and physical, especially cellular biochemical physiological mechanisms; individual plant sensitivity/ genetic composition; site/habitat influences; pest, disease, and abiotic stress interactions.
- **Ecosystems:** increase understanding of the exposure/response relationships of sensitive individual plant species and forest trees to ozone, under ambient conditions, characterize the impact of exposure on interspecies competition on both above and below ground interactions and on ecosystem products and services.
- **Assessment:** assessment of economic impacts on products (crops, forests, etc.) and ecosystem services, benefits derived from control of ozone exposures. Removal of as many of the uncertainties cited above as possible will benefit and assist EPA in developing a secondary NAAQS for ozone that will protect vegetation.

Real time data for verification of actual exposures is lacking. The continuing lack of air quality monitoring data to characterize actual ozone exposures across broad regional expanses of rural, agricultural, and remote forested areas is of great concern. Paucity of air quality monitoring data had always hampered the characterization of rural and remote air quality on a regional and national basis. Many of the monitors classified as rural are located within cities or Census Metropolitan Statistical Areas (CMSA's), and often indicate ozone air quality patterns typical of urban areas (e.g., low nighttime ozone due to scavenging, with high diurnal peaks,

frequently including occurrences of hourly averages above 0.10 ppm). Diurnal patterns can differ significantly between urban and rural areas. Both Kriging and GIS based approaches can be used to predict exposures in rural areas where no monitors exist, but these methods should be validated with augmented monitoring data.

The research needs presented in this document do not constitute a specific research program or research plan. Rather, as mentioned above, these needs are intended to provide a broad conceptual context, within which specific research programs and plans can be developed. In this regard, the research approaches mentioned under some specific research needs should not be taken to constitute predictions of specific future requests for proposals issued by U.S. EPA or any other sponsoring organization. Rather, consistent with the broader scope and spirit of this document, they are presented as springboards for further thought and discussion.

In its letter of January 29, 1999, the CASAC stated: "The Panel proposes the recommendations for particulate matter research developed by the National Research Council [NRC] as an example of the scope of integration and prioritization that the Agency needs to apply to ozone information needs." The NRC research portfolio addresses information needed for both the standard-setting process and for effective implementation of standards. The purview of the present document, however, is limited to broad informational needs to support the standard-setting process. Within this limitation, the present document endeavors to achieve conceptual consistency between ozone research needs and the needs presented in the NRC research portfolio for PM. The NRC research portfolio for PM includes suggested time lines for PM research. The present document does not include time lines for ozone research. Any such time lines are more appropriately presented in a companion document to this one, which delineates the EPA's Office of Research and Development (ORD) strategy for ozone-related health and ecological research.

CHAPTER 2. RESEARCH NEEDED TO REDUCE UNCERTAINTY IN HEALTH RISK ASSESSMENT FOR OZONE

2.1 INTRODUCTION

Experimental studies have demonstrated pulmonary changes in laboratory animals, including primates, in response to long-term exposure to realistic ambient ozone concentrations. Effects of major concern occur in the respiratory bronchiolar-alveolar transition region (centriacinar region), where ozone-induced histopathologic changes and small-airways remodeling (thickening of respiratory bronchioles and lengthening of the respiratory bronchiolar region) are both observed. These changes involve anatomic structures, tissue types, and cell types that are all present in the human lung, and that could all plausibly be affected by long-term ambient ozone exposure. If similar changes occur in humans, they could well be associated with notable pathophysiologic sequellae, including increased small-airway resistance, reduced pulmonary gas-exchange surface and oxygen diffusing capacity, and ventilation-perfusion mismatches. Such changes could also affect the ozone dose in different lung regions, and the dose distribution among regions. Severe, progressive changes could be associated with clearly harmful outcomes such as shortness of breath (dyspnea), hypoxia, accelerated long-term lung function loss in adults, retarded lung function growth in children, and, conceivably, clinically apparent chronic lung disease.

Epidemiologic studies also show changes associated with long-term ambient ozone exposure that are consistent with the histopathologic and micro-anatomic changes mentioned above, and with their potential pathophysiologic and clinical sequellae. Briefly, a pilot autopsy study in southern California has shown pulmonary centriacinar pathology in about 80%, and severe pathology in over 25%, of young adults who died in accidents. Another study, though inconclusive, suggests that adults' lung function may decline faster in high-ozone communities than in low-ozone communities. Also of concern are recent observations of reduction in small-airways spirometric parameters in college students, and increased asthma incidence in adult males, who live in areas with relatively high ambient ozone levels.

A growing body of evidence also shows associations of short-term ambient ozone exposure with deleterious changes in health. In several recent epidemiologic studies, associations of

elevated ambient ozone levels with elevated daily mortality counts have been observed. In some of these, associations of ozone with mortality have been as statistically robust as associations of particulate matter (PM) with mortality. Associations of short-term ozone elevations with increased frequency of respiratory hospitalization and emergency room visits, mainly in asthmatics, have also been observed repeatedly. Clinical studies suggest that in asthmatics at least, ozone-induced reduction in spirometric lung function may persist for many hours. Clinical studies of physiologic and intrabronchial pathologic, cellular-inflammatory, and biochemical parameters have revealed differences between asthmatics' and non-asthmatics' responses to short-term ozone exposures. For example, more intrabronchial inflammation is observed in asthmatics than non-asthmatics at 18 hours after cessation of chamber ozone exposure. Available evidence suggests further that ozone-induced lung inflammation and tissue injury may persist after acute physiologic responses have returned to baseline.

Current evidence shows that the occurrence and severity of ozone-mediated health effects are not simple functions of cumulative ozone exposure, or even of cumulative inhaled dose. For example, in primates, different histopathologic centriacinar effects were observed with continuous versus alternate-monthly long-term exposure to 0.25 ppm ozone, and these effects were more severe in some ways with intermittent exposure (smaller cumulative dose). These and other findings suggest that ozone-induced tissue injury may persist after cessation of ozone exposure, that the balance of tissue injury and repair may differ with continuous and intermittent exposure, and that repair processes are not always harmless. Such findings also indicate that results of continuous-exposure studies provide only uncertain grounds for extrapolation to ozone effects in the real world, where ambient ozone levels generally vary substantially both within days and across seasons and years.

A fundamental goal of health risk assessment for ozone, as for any environmental pollutant, is to characterize and quantify the public health burden that ambient exposure confers and that ozone reduction would prevent. In the framework of public health and epidemiology, risk characterization requires knowledge of both the relative risks and attributable risks associated with ambient exposure. Briefly, the relative risk associated with a given exposure (e.g., to ambient ozone) is the ratio of health risk in persons with higher exposure to the risk in persons with lower exposure (including unexposed persons). To characterize relative risks of ambient ozone exposure, it is necessary to identify the nature of ozone-induced health effects, then to

develop exposure-response (or ideally, exposure-dose-response) relationships for the population as a whole and for ozone-susceptible subgroups. These relationships should be developed as quantitatively as possible. To characterize relative risks, exposure assessment studies, experimental health studies, animal-to-human extrapolation, and epidemiologic studies are all required.

The attributable risk associated with an exposure is *the number of persons* in whom the health disorder can be ascribed specifically to the exposure. The concept of attributable risk is closely related to the concept of public health burden. Characterization of attributable risks requires accurate knowledge of relative risks, the sizes of population groups experiencing different levels of ambient ozone exposure, and the actual levels of exposure that these groups experience. Exposure assessment studies and epidemiologic studies are required in this effort.

Current uncertainties in the ozone health and exposure data bases impede comprehensive, quantitative health risk assessment regarding prolonged ozone exposure. These uncertainties must be resolved to ensure that ambient ozone regulations are duly protective of public health but not unduly stringent. Major existing uncertainties are discussed below, first regarding the relative-risk aspect, then regarding the attributable-risk aspect of ozone health risk assessment.

As mentioned above, there is considerable reason for suspicion that prolonged ambient ozone exposure may induce chronic pulmonary pathology in humans. However, this has not been confirmed. The mechanisms and time courses of tissue injury, repair, and remodeling through which ozone exposure produces histopathologic and anatomic changes in the centriacinar and other anatomic regions, have not been fully characterized even in laboratory animals. (Indeed, the basic mechanisms of injury and repair, and the positive and negative consequences of repair, are not fully understood, irrespective of environmental pollution effects upon these processes.) The long-term progression (natural history) of ozone-induced histopathologic changes, and dosimetric and pathophysiologic consequences at different stages of their development and progression, also remain to be determined. In future research, it will be essential both to identify these outcomes, and to characterize and compare the influences of different exposure concentrations and time courses (including continuous vs. intermittent exposure) upon them.

Epidemiologic and experimental studies, though necessary, will not be sufficient to quantify the public health consequences of long-term ozone exposure. These studies should be

supplemented by quantitative extrapolation of results obtained in laboratory animal studies to the human population. Extrapolation studies will be necessary to establish linkage between laboratory animal studies and human studies. Therefore, it is important to continue development and validation of animal models for extrapolation, and to improve methods of extrapolating biological effects across species. Because biological effects induced by ozone exposure are highly diverse, and because extrapolations may differ appreciably for different endpoints, a variety of studies, each employing appropriate exposure schedules and appropriate specific health-related endpoints, should be conducted in this effort.

Available experimental evidence shows that identical ozone exposure schedules elicit different degrees of response in different individuals, and thereby confirms the existence of differential sensitivity to ozone exposure. However, even after decades of research, the host and environmental factors responsible for differential short-term ozone sensitivity are not well understood. Relationships of exposure with dose delivered to and absorbed by target cells and tissues, and relationships of dose with the presence and severity of biological effects, require much further characterization. Influences of prior ozone exposure on current ozone dose and response are also incompletely understood, as are influences of prior and current ozone exposure on response to other environmental substances.

There also remains uncertainty as to relationships of short-term ozone-induced *response* with true ozone-induced *injury and pathophysiology*, and with long-term impairment of health. Further research on this issue is required both to advance understanding of short-term and long-term ozone health risks, and to develop short-term or early markers of potentially-adverse long-term effects. Somewhat ironically, the well-known phenomenon of attenuation ("adaptation") of some, but not all, types of acute response after repeated ozone exposure complicates these issues, but also offers opportunities to address them effectively in future research.

Accurate identification of ozone-sensitive subpopulations, and specific characterization of their ozone-associated health risks, requires knowledge of host susceptibility factors. There remains much uncertainty in this area. Experimental studies have begun to identify genetic influences on ozone response, but further research is required on this topic. Current evidence also suggests relationships of endogenous and ingested antioxidants (including vitamins C and E) with ozone response, but these, too, have not been well characterized. Influences of demographic factors, and of personal habits such as smoking, also remain to be determined.

It is accepted that asthmatics constitute an ozone-susceptible population. One published paper also describes an association of long-term ambient ozone exposure with incidence of new asthma cases in adult males. At the same time, the specific influences of ozone exposure on asthma incidence and exacerbation are not yet understood. Also, the observed association of long-term ozone with asthma incidence is not confirmed. Because asthma incidence and mortality are probably both increasing in the U.S., it is especially important to improve understanding of ambient ozone and asthma. Additionally, there is a pressing need to characterize the specific influences of ambient ozone exposure on mortality and shortening of lifespan.

The attributable-risk aspect of ozone risk assessment is also subject to much uncertainty. The magnitudes of past and present ambient ozone exposure in the whole population, and in sensitive subpopulations, have not been fully characterized. It is not feasible to measure ozone exposures directly in all relevant subpopulations. Rather, it will generally be necessary to estimate exposure from central fixed-site ozone measurements. Further development and evaluation of ozone exposure models will be required for this purpose.

To date, most experimental ozone health research has been conducted using ozone alone. However, ozone does not—indeed cannot—occur as the sole ambient oxidant air pollutant. Also, ambient concentrations of ozone and co-pollutants exhibit much spatial and temporal variation. There is increasing realization that air pollution-associated health effects in the population often arise from multi-pollutant exposure, not simply from exposure to ozone or any other single pollutant. Thus, further multi-pollutant health research is badly needed. Such research will be required in the areas of both exposure assessment and health effects. Comprehensive consideration of multi-pollutant research issues is beyond the scope of this document. However, full understanding of the health risks of ozone, or any other single pollutant, will require further understanding of multi-pollutant effects. Such understanding will also be necessary to understand the health benefits that would result from selective reduction of ozone or any other single pollutant. From the standpoint of ozone health risk assessment, co-pollutants of major concern include particulate matter (PM), nitrogen oxides and other photochemical oxidants, and aeroallergens.

In summary, current scientific evidence strongly suggests that ambient ozone exposure has imposed, and may continue to impose, a substantial burden on public health. That burden has

not yet been fully described quantitatively or even qualitatively. Sufficient understanding of that burden will require much further experimental and epidemiologic research on ozone, both alone and in combination with other environmental substances. Specific health-related research needs for ozone are discussed below in Section 2.2.

2.2 DISCUSSION OF OZONE HEALTH-RELATED RESEARCH NEEDS

1. Improve understanding of human exposures to ambient ozone and to related, potentially harmful air pollutants.

1a. Gather population-based information on total human ozone exposure, sufficient to evaluate current and future ozone exposure models.

Advanced probabilistic methods already exist for population-based modeling of ambient ozone exposure in support of setting ozone air quality standards. These methods have been reviewed extensively and accepted by CASAC. Even so, confidence in existing models, like any environmental models, will be increased by evaluation and verification with empirical data. Outputs from probabilistic ozone exposure models are estimated distributions of ozone exposure in the general population, or in specific subpopulations of interest (e.g., children, outdoor workers, or other ozone-sensitive subpopulations yet to be discovered). To evaluate these models, it is necessary to obtain measured distributions of total personal ozone exposure in such population groups.

There remains a distinct shortage of the ozone exposure measurements required to characterize population-based exposure distributions in the real world. Obtaining the necessary information will require field studies designed to collect sufficient information on total personal ozone exposure. In these studies, representative samples of the general population and of specific subpopulations should be selected, and total personal ozone exposure should be measured in sample members. The duration of these field studies should be long enough to allow effective evaluation of exposure models throughout the high-ozone season at a minimum. Also, measurements should be frequent enough to allow ascertainment of ozone exposure distributions at hourly intervals. These field studies will require considerable supplementation of existing ambient ozone monitors with personal ozone monitoring and with stationary monitoring in the outdoor and indoor microenvironments in which sample members conduct their activities.

Ideally, these studies would be conducted not only for ozone, but also for ozone in combination with other air pollutants (e.g., PM).

1b. Gather information needed to improve inputs to current and future population-based ozone exposure models.

Additional information is needed to reduce the uncertainties associated with some types of inputs to current and future probabilistic ozone exposure models. For example, one important type of input is indoor-outdoor time-activity information. Setting of appropriate air quality standards for ozone (and for other air pollutants) will be facilitated by accurate exposure estimation for multiple population groups, in multiple locations, in different seasons, and in different years. Time-activity information is currently limited to only a very few days for each person. Collection of time-activity data over longer time periods is needed to reduce uncertainty in the modeled exposure distributions that form an important part of the basis for decisions regarding air quality standards for ozone (and other air pollutants).

Other types of exposure model inputs for which additional information is needed include indoor and in-vehicle air exchange rates, information on presence of air conditioning, times when windows and doors are open, and indoor-outdoor relationships of airborne ozone concentrations. Augmentation of all of these types of information would reduce uncertainty in the ozone exposure modeling process. At the same time, setting specific priorities among these types of inputs will depend largely on the results of field studies designed to evaluate model performance (see research need 1a., above). For example, results of the model evaluation studies could conceivably indicate that models accurately estimate ozone exposure distributions in one location, even if the models employ air exchange rate information from other locations. These studies could also conceivably indicate that location-specific time-activity information is necessary for accurate location-specific estimation of ozone exposure distributions. If so, higher priority should be given to augmenting the database for time-activity patterns than for air exchange rates.

The foregoing discussion has focused on modeling of population-based ozone *exposure distributions*. The standard setting process would gain scientific strength and credibility if more accurate estimation of population-based *inhaled dose distributions* could also be achieved for ozone and other air pollutants. Ascertainment of inhaled dose requires knowledge not only of

airborne pollutant concentration, but also of the volumes of air that persons breathe over time (time-specific ventilation rates). Currently, little information on ventilation rates is available at the community level. Further research is needed to enhance this information. This research should include direct measurement of ventilation rates in various population groups in various locations, across the spectrum of physical activity from rest (including sleep) to vigorous exercise. The utility of surrogate metrics for ventilation (e.g., heart rate) should also be explored.

1c. Improve understanding of atmospheric chemistry involving ozone, as needed to improve understanding of human exposure to ozone, particulate matter, and other potentially harmful air pollutants at the community level.

There remains much to be learned regarding indoor and outdoor atmospheric chemistry that involves ozone and other air pollutants. Aspects of atmospheric chemistry that are relevant to air pollution health effects research, and that require augmentation, include the following: further characterization of chemical reactions, involving ozone and other gaseous pollutants, that may generate or remove airborne particles; further characterization of gas-phase reactions that generate ozone or remove it from outdoor and indoor air; and further characterization and monitoring of airborne oxidant air pollutants that may have harmful health effects (e.g., peroxyacylnitrates or other heavily oxygenated air pollutants).

The stratospheric ozone layer plays an essential role in filtering harmful ultraviolet sunlight. Conceivably, tropospheric ozone could also filter some ultraviolet sunlight. If so, the presence of tropospheric ozone could conceivably confer some health benefit. Therefore, the role of tropospheric ozone in filtering ultraviolet sunlight should be ascertained. If tropospheric ozone is shown to filter ultraviolet radiation to a detectable degree, its potential health benefits should also be characterized.

1d. Explore the utility of applying emissions-based ozone air quality modeling methods (currently used at the regional scale for attainment/compliance purposes) to the neighborhood scale, in order to provide supplemental assessment of human exposure to ambient ozone.

To date, emissions-based air quality models have been used primarily for assessing attainment of and compliance with air quality standards in large geographic areas. Conceivably, emissions-based modeling techniques could be adapted to estimate ambient concentrations of ozone and other air pollutants at the neighborhood level. The feasibility of such adaptation

should be explored. If it proves feasible, these neighborhood-level estimates could prove useful in estimating ambient air pollution exposures for subjects in large health surveys (e.g., the National Health and Nutrition Examination Surveys [NHANES]) that do not include direct air pollution monitoring data. Such emissions-based neighborhood air pollution estimates might prove especially useful for estimating exposures of subjects in geographic areas that do not have ambient air pollution monitors.

2. Improve understanding of health effects of long-term ozone exposure.

As discussed above, there are ample grounds for scientific concern that long-term ambient ozone exposure exerts harmful health effects. However, there remains much uncertainty as to the duration of exposure required to exert such effects, the "patterns" of exposure most instrumental in exerting such effects (e.g., are intermittent peak exposures more harmful than continuous low-level exposure?), and even as to the nature of the health effects themselves. Therefore, there is an urgent need to advance understanding of health effects of long-term exposure to ambient ozone. Both experimental and epidemiologic studies will be required to address this need.

2a. Experimental studies of long-term ozone exposure.

Further experimental studies should be conducted to characterize long-term health effects of exposure to ozone alone and in combination with other environmental substances (e.g., air pollutants and aeroallergens). These studies should address long-term changes in the centriacinar region of the lung. Topics for study should include ascertainment of the ozone exposure patterns most instrumental in producing centriacinar changes, and the time course to the various histopathologic changes in the centriacinar region. Physiologic and pathologic sequelae of these changes should be described. The degree of histopathologic, pathophysiologic, and pathologic reversibility of such changes should be ascertained. Ozone effects outside the centriacinar region should also be characterized further.

Ozone responses in animal models of asthma should be compared to those in non-asthmatic animals. Experimental research that employs joint exposure to ozone and aeroallergens (or ingested allergens) should be continued, in order to advance understanding of ambient ozone effects in human asthmatics.

Harmful long-term health effects may result from repeated short-term ozone exposures. Also, short-term ozone exposure causes short-term reductions in lung function in experimental studies, and has consistently been associated with similar reductions in epidemiologic studies. Such short-term physiologic changes have figured prominently in regulatory decisions on ozone. These changes are clearly harmful in asthmatics, whose baseline lung function is already low. However, the extent to which such changes may predict increased incidence of overt illness remains uncertain. Further studies are needed to determine the degree of association of short-term physiologic change with long-term risk of overt illness.

2b. Epidemiologic studies of long-term ozone exposure.

Recent scientific publications have shown that health effects of long-term ambient ozone exposure can be effectively assessed in epidemiologic studies, if appropriate study designs are employed in appropriate study settings. These studies should be continued and enhanced. The most important research questions include the following: Does long-term ozone exposure promote development of asthma or chronic obstructive pulmonary disease?; Does long-term ozone exposure promote shortening of human lifespan via promotion of such diseases?; What annual and seasonal patterns of long-term ozone exposure are most instrumental in promoting harmful health effects?; Does "adaptation" to repeated short-term ozone exposure actually increase the long-term dose of ozone, and thereby increase disease risk in persons who "adapt"? Meticulous assessment of long-term exposure to ambient ozone and PM has been a strength of some recent epidemiologic studies. Future studies of long-term ozone exposure should continue to employ such assessment. This assessment should also be extended to other airborne substances, e.g., aeroallergens. Long-term epidemiologic studies should incorporate careful assessment of nutritional, socioeconomic, and demographic factors.

2c. As feasible, develop and validate biomarkers of subchronic and chronic ozone exposure and effects in experimental and epidemiologic studies.

In recent years, much attention has been devoted to identification of biological markers (biomarkers) of exposure to, and effects of, environmental pollutants. In some instances, sensitive and specific biomarkers have been successfully identified. When this has proven possible, employment of biomarkers as surrogates for exposures or effects has assisted in

environmental health research and risk assessment. Theoretically, biomarkers of ozone exposure or effects would be very useful, because ozone itself is highly reactive and therefore does not persist in the body over the long term. At the same time, experience has shown that identification of effective biomarkers is difficult in the field of ambient air pollution health research. This is true largely because the health effects of ambient air pollution are not specific to exposure to one or another pollutant. In the future search for ozone-related biomarkers, attention could be focused on identification of ozone reaction products in respiratory tract cells, tissues, or fluids as biomarkers of long-term ozone exposure. The sensitivity and specificity of any putative biomarkers should be systematically characterized.

3. Improve understanding of health effects of short-term ozone exposure.

As discussed below under research needs 3a. and 3b., there are two primary reasons for augmenting research on the health effects of short-term ambient ozone exposure. First, in persons with pre-existing disease, short-term ambient ozone exposure may produce harmful health effects. However, there remains some uncertainty as to the nature of these effects, and much uncertainty as to the quantitative relationships between ambient ozone exposures and the frequencies of these effects. Second, it is quite conceivable that repeated, elevated short-term or medium-term ambient exposures may be largely responsible for harmful chronic effects of ambient ozone. Further research on effects of short-term and medium-term ozone exposures will be necessary to ascertain whether this is true. Thus, further study of short-term ozone exposure is important not only to improve understanding of short-term exposure effects per se, but also to improve understanding of the cumulative health effects of repeated short-term exposures.

3a. Experimental studies of short-term ozone exposure.

Experimental and epidemiologic studies have shown that ozone exposure, even at low levels, produces short-term reductions in lung function in a substantial portion of the population. It is not yet clear, however, whether such reductions are fully reversible. If not, repeated ozone-induced lung function reductions could bring about permanent loss of lung function, retardation of lung function growth rate in children, or acceleration of lung function loss rate in adults. In epidemiologic studies, permanent loss of lung function has been associated consistently with increased mortality from pulmonary and cardiac diseases.

Therefore, there is an important need to ascertain whether repeated short-term ozone-induced reduction in lung function promotes permanent lung function deficits. Further experimental studies, employing repeated short-term ozone exposures over the long term, will be important in addressing this research need effectively. In these studies, ozone should be assessed alone and in combination with other air pollutants, e.g., PM.

If repeated short-term ozone exposure is indeed responsible for chronic ozone-induced health effects, it will be necessary to ascertain specific biological pathways through which these chronic effects develop. One possibility in this regard is that short-term ozone exposure may promote acute respiratory infection (ARI). Conceivably, repeated ARIs could predispose to development of long-term, relatively irreversible pulmonary disease. Thus, relationships of short-term ozone exposure with ARI should be explored further.

Also, available evidence suggests that under some conditions, ozone and airborne allergens can act synergistically in producing exacerbation of pre-existing asthma. However, the current database is not wholly consistent on this important issue. Further experimental study of the interplay of ozone (and other pollutants) with allergens is needed.

3b. Epidemiologic studies of short-term ozone exposure.

As discussed above, available epidemiologic studies suggest an association of short-term ambient ozone levels with short term elevations in daily mortality. Current evidence suggests that ambient PM may be more important than ozone in promoting these elevations. However, the existing epidemiologic database does not reflect even-handed scrutiny of ozone and other air pollutants. Specifically, more attention has been devoted to assessing PM effects than ozone effects on mortality. Therefore, the actual absolute and relative contributions of ambient ozone to daily mortality remain uncertain. Future epidemiologic studies of ozone and daily mortality should be conducted, and even-handed consideration should be given to multiple air pollutants.

Short-term elevations in ambient ozone concentration have also been associated with exacerbation of pre-existing asthma. The evidence for a specific linkage between ambient ozone and asthma exacerbation is somewhat more solid than that for ozone and daily mortality. Even so, the relative roles of ozone and other air pollutants in asthma exacerbation are not yet clear. Future epidemiologic studies of asthma, as of mortality, should give even-handed consideration to multiple pollutants.

To date, most epidemiologic studies of effects of short-term exposure to ozone and other air pollutants have been time series studies in large populations. Important advances in statistical analysis of time series data have recently been made. Even so, time series studies remain subject to some uncertainty due to incomplete data on air pollution levels or health outcomes, to limitations in existing statistical methods, or to a combination of these. A growing number of air pollution studies other than time series studies (e.g., case-crossover studies, panel studies) is appearing in the scientific literature. This trend is to be encouraged in future epidemiologic research on short-term ozone exposure.

In population time series studies of ozone and other ambient air pollutants, independent variables for air pollution have generally been measurements made at stationary outdoor monitors. The accuracy with which these measurements reflect subjects' actual pollution exposures is not yet adequately understood. Also, there has not yet been adequate characterization of the degree to which discrepancy between stationary-monitor measurements and actual pollutant exposures introduces error into statistical estimates of pollutant effects in time series studies. Further characterization of these exposure-related errors should be conducted in concert with future epidemiologic studies of ozone and other air pollutants.

3c. Develop and validate biomarkers of short-term ozone exposure and effects in experimental and epidemiologic studies.

Research to identify biomarkers of short-term ozone exposure and effects should continue. This research should include identification of reaction products of short-term ozone exposure in the respiratory tract (see research need 4c., below). As with putative long-term biomarkers, the sensitivity and specificity of putative biomarkers of short-term ozone exposure and effects should be systematically characterized.

4. Improve understanding of ozone dosimetry and augment interspecies extrapolation of ozone effects.

4a. Among different species, further characterize and compare inherent sensitivity to ozone, and ozone dosimetry in different respiratory tract regions.

Studies in humans and laboratory animals are both essential to gain further understanding of the health effects of ambient ozone. At the same time, the degree to which findings of

laboratory animal studies can be extrapolated to humans remains uncertain. Reduction of this uncertainty would enhance the contribution of laboratory animal studies to ozone risk assessment, and would provide useful guidance for future laboratory animal studies.

In any given species, the nature and severity of ozone-mediated health effects depends on both inherent ozone sensitivity and ozone dose. Two species with different inherent sensitivities will develop different health effects if they receive the same ozone dose. Also, two species with similar inherent sensitivities will develop different effects if they receive different ozone doses. Knowledge of both inherent sensitivity and dose is essential to provide an adequate basis for effective interspecies extrapolation.

There remains a distinct shortage of information regarding inherent ozone sensitivity and ozone dosimetry in different species. For example, in any given species, it is difficult or impossible to develop quantitative dosimetric estimates without knowledge of the regional anatomy of the respiratory tract. To date, however, regional respiratory anatomy has not been fully described for any single animal species.

Thus, there is a definite need for further research to augment the empirical database for interspecies extrapolation of ozone health effects. The purpose of this research should be to advance understanding of both inherent ozone susceptibility, and ozone dosimetry, in various species. Advancement of interspecies extrapolation models for ozone is also needed.

4b. Characterize ozone mass transfer coefficients in different regions of the respiratory tract.

The critical aspect of ozone dose is probably not the amount of ozone within the airways, but rather the amount that encounters the respiratory fluids and tissues at the cross-sectional boundaries of the airways. To ascertain this "critical dose," it is necessary to determine mass transfer coefficients for ozone from within the airways to the ozone-fluid-tissue interface. These coefficients should be determined for different regions of the respiratory tract. To support effective interspecies extrapolation, they should also be determined in a variety of species.

4c. Improve understanding of chemical reactions of ozone in the respiratory tract, especially in the lung lining fluids. Ascertain short-term and long-term biological processes triggered and influenced by ozone and its reaction products.

As mentioned above, ozone is highly chemically reactive. When it encounters respiratory fluids and tissues, it is very likely to react with them, thereby creating new reaction products. These intermediate reaction products may actually be directly responsible for a significant portion of ozone-mediated toxicity. Thus, in future research it will be important to characterize these products further, and to advance understanding of the biological processes that they influence. Also, these reaction products could be evaluated as putative short-term biomarkers for ozone. Conceivably, biologically active reaction products could serve as joint markers of both ozone exposure and ozone effect (see research need 3c. above).

5. Identify subpopulations susceptible to ambient ozone and characterize health effects of ozone and co-pollutants in these subpopulations.

5a. Experimental studies of ozone susceptibility.

It is well known that lung function response to experimental ozone exposure varies widely among test subjects. The airways inflammatory response to such exposure also exhibits considerable interindividual variation. Gender does not appear to be an important susceptibility factor for short-term lung function response. Also, African-Americans and Caucasians do not differ substantially in lung function response to short-term experimental ozone exposure. Beyond this, the factors that influence short-term susceptibility are not known. Further experimental research, in both humans and laboratory animals, is needed to identify these factors.

Also, it is not yet known whether susceptibility to effects of short-term ozone exposure is associated (positively or negatively) with long-term ozone susceptibility. Further experimental studies are needed to explore this important issue. This research could include an effort to ascertain whether specific genetic markers are associated with short-term and long-term ozone susceptibility and, if so, whether the markers for both types of susceptibility are the same. Further research is also needed to ascertain whether physiologic "adaptation" to repeated short-term ozone exposure is related to increased susceptibility to chronic ozone-mediated health effects. Further development of ozone-susceptible laboratory animal models is also needed.

5b. Epidemiologic studies of ozone susceptibility.

As discussed above, the nature and severity of ozone-mediated health effects depends on both inherent ozone sensitivity and ozone dose. Similarly, human susceptibility to ozone and other pollutants at the community level depends on both inherent predisposition to health effects (host factors) and exposure. For example, a person or group with high inborn predisposition to ozone effects would not experience harmful effects unless actually exposed to ozone. Conversely, a person or group with low inborn predisposition might experience little or no harmful ozone effects, even if exposed to substantial amounts of ozone. Further epidemiologic studies are needed both to characterize the host factors associated with susceptibility to short-term and long-term ozone exposure, and to characterize the relative importance of host factors and exposure in promoting ozone-associated health effects. The roles of demographic, socioeconomic, genetic and nutritional factors should be investigated. Exposure to ozone and other air pollutants should be thoroughly and even-handedly assessed in all studied groups.

6. Determine biological mechanisms of injury induced by ozone alone, and by ozone in combination with co-pollutants.

6a. Further characterize the nature and time course of ozone-induced cellular and tissue injury.

Recent years have witnessed important advances in understanding of cellular and tissue injury by ozone and other air pollutants. Even so, further research is needed in this area. For example, the degree to which short-term (partially reversible) injury is linked to chronic (possibly irreversible) injury is not fully understood. The time course of tissue remodeling, and the mechanisms through which it occurs, require further study. Similarly, there remains uncertainty as to the relationship of pollution-mediated cellular and tissue injury and clearly harmful health effects. Also, the relation of injury severity to the pattern of exposure (not merely the amount of exposure) requires further characterization. In future research, exposure protocols should include ozone alone and in combination with other pollutants. Susceptibility of different population groups to ozone-mediated cellular and tissue injury should be characterized further. The research recommended here will advance understanding not only of ozone effects, but of oxidant injury in general.

6b. Further characterize the nature and time course of sequelae of ozone-induced injury.

Many types of tissue injury are followed by tissue repair and healing. The consequences of these sequelae of injury are not always entirely beneficial. In many cases, for example, "tissue repair" brings about changes in both the types and organization of tissues at and around the site of injury. In the lung, tissue repair may involve replacement of healthy epithelium and structural proteins with scar tissue (fibrosis). When this occurs both effective gas exchange and mechanical lung function are compromised. It will be important to gain further understanding of factors which influence the balance between beneficial and non-beneficial sequelae of injury mediated by ozone and other air pollutants.

7. Characterize health benefits of reduction of exposure to ambient ozone and other air pollutants.

Thorough risk assessment provides the best possible scientific estimate of the health effects of exposure to ambient ozone and other environmental pollutants. It also provides the best possible scientific prediction of the health benefits that would be achieved by standards for ozone and other pollutants. At the same time, though risk assessment predicts health benefits of regulation, it does not, indeed cannot, characterize these benefits directly. Such characterization requires research and population surveillance focused on ascertaining the actual health benefits of environmental pollution reduction.

To date, the great majority of environmental health research has concentrated on effects that occur when pollutant exposure is present, or when it is increased. There is need for additional research that concentrates on benefits (if any) that ensue when such exposure is reduced or eliminated. This additional research and surveillance is very important because the overall system in which environmental regulation takes place is exceedingly complex. Truly quantitative establishment of health benefits is therefore generally beyond the capability of risk assessment conducted before regulation.

Adequate characterization of health benefits of reduction of exposure to ozone and other pollutants will require experimental research, and epidemiologic research and surveillance. Needs in these areas are discussed briefly below. Hopefully, the discussion here will serve to stimulate further thought and implementation in this important field. At the same time, it is emphasized that full consideration of this topic is beyond the scope of this document.

7a. Conduct experimental studies designed to assess health benefits of reduction of exposure to ozone and other environmental pollutants.

As mentioned above, most existing health-related studies of O_3 have involved addition of O_3 to experimental test systems. There is need for additional studies in which O_3 is first present in the test system, and is subsequently reduced or eliminated. By studying exposure reduction, these studies could simulate exposure characteristics when ambient pollutant standards are implemented. Such studies could be useful in ascertaining the nature and time course of benefits that occur, at the histopathologic, pathophysiologic, and pathologic levels, when exposure is reduced. These studies could be designed to characterize benefits of long-term and short-term reduction of exposure to ozone alone and to multi-pollutant mixtures that contain ozone.

7b. When feasible, conduct epidemiologic studies and population surveillance in locations that experience reduction in ambient ozone concentrations.

Standards for ozone and other criteria air pollutants are implemented primarily to protect public health. Risk assessment enables prediction of the public health benefits that such standards will provide. Direct observation of changes in health status in the population, after implementation of standards, would be necessary to ascertain the actual nature and degree of public health benefit that such standards provide. To date, little effort has been devoted specifically to such assessment after regulation. Thus, while previous air quality standards have undoubtedly benefitted public health, the actual degree of benefit that they have conferred is uncertain. In the future, the effort to ascertain the public health benefits of O_3 standards and other environmental pollutants should be augmented at the population level. This effort should include ascertainment of both pollutant exposure reductions and health benefits that follow implementation of standards. Admittedly, this effort will be difficult because, as mentioned above, the overall system is very complex and relevant health outcomes are not specific to one or another air pollutant. Even if ambient O_3 and other air pollutants were eliminated, frequency of these outcomes in the population would not fall to zero. Nevertheless, with choice of appropriate study designs and study settings, progress can be made in evaluating the real-world consequences of air quality standards for O_3 and other air pollutants. In this effort, it will be important to ascertain, as scientifically feasible, the degree to which implementing O_3 NAAQS reduce the incidence of asthma and COPD and prevent air pollution-mediated shortening of human lifespan.

CHAPTER 3. RESEARCH NEEDED TO ASSESS OZONE EFFECTS ON CROPS, FORESTS, AND NATURAL ECOSYSTEMS

3.1 INTRODUCTION

The objective of future research on the effects of ozone on agricultural crops, natural and plantation forests and native vegetation and wildlife components of terrestrial and aquatic ecosystems is to minimize the current uncertainties in establishing exposure/response relationships under ambient conditions. A review of the OAQPS Staff Paper (EPA-452/R-96-007, June 1996) indicates that uncertainties that existed in data in a number of categories increased the uncertainties associated with developing qualitative and/or quantifiable risks to various components of agronomic, forested and natural ecosystems. These uncertainties in the data made difficult selection of a secondary standard that would protect crops, forests, natural vegetation and ecosystems. Four categories where additional information is needed include the following: *Exposure Dynamics*: monitoring to determine ambient ozone concentrations encountered in urban, rural farm/forest/wetland areas, exposure patterns (episodes), concentrations vs flux, relationship between chamber and field exposure data, plant uptake; *Response/Mode of Action*: biological, chemical and physical, especially cellular biochemical physiological mechanisms; individual species sensitivity/ genetic composition; site/habitat influences; pest, disease, and abiotic stress interactions; *Ecosystems*: increase understanding of the exposure/response relationships of sensitive individual species to ozone, under ambient conditions, and characterize the impact of exposure on interspecies competition on both above and below ground interactions and on ecosystem products and services. *Assessment*: of economic impacts of ozone on plant products (biomass and yield of crops, forests, etc.) and ecosystem services, and benefits derived from control of ozone exposures. Removal of as many of the uncertainties cited above as possible will benefit and assist EPA in developing a secondary NAAQS for ozone that will protect vegetation.

Real time data for verification of actual exposures is lacking. The continuing lack of air quality monitoring data to characterize actual ozone exposures across broad regional expanses of rural, agricultural, and remote forested areas and wetlands is of great concern. Sparse air quality monitoring data has always constrained the characterization of rural and remote air quality on a

regional and national basis. Many of the monitors classified as rural occur within cities or Census Metropolitan Statistical Areas (CMSA's), and often indicate ozone air quality patterns typical of urban areas (e.g., low nighttime ozone due to scavenging, with high diurnal peaks, frequently including occurrences of hourly averages above 0.10 ppm.) Diurnal patterns can differ significantly between urban and rural areas. Both Kriging and GIS based approaches have been used to predict exposures in rural areas where no monitors exist.

The response of vascular plants to ozone may be viewed as the culmination of a sequence of physical, biochemical, and physiological events. Exposure dynamics involve the movement of ozone from the atmosphere into a plant canopy, its absorption to surfaces (stems and leaves), into leaf tissues and onto soil. Many studies over the years, depending on the timing and duration of the episode(s), plant sensitivity and stage of plant development, have shown that injury to crops, some native forest trees and understory vegetation, can occur when exposed to ozone concentrations ranging from 0.04 to 0.4 ppm, with the highest concentrations, especially peaks > 0.09 ppm, causing injury in the shortest period of time. Peak concentrations in general have been implicated as being the most important in causing plant injury. However, some studies suggest that exposure patterns with variable concentrations that include peaks, produce the greater effects. Still other studies suggest that "mid-range concentrations" (0.05 to 0.09 ppm) are more important in producing plant effects. At present, long-term cumulative exposures composed of mid-range and peak concentrations are considered to relate most closely to vegetation response.

No threshold ozone concentration or cumulative seasonal exposure has been identified above which effects for all plant species occur or below which they do not occur. Exposure/response relationships for ozone and plants have usually been established by using mean concentrations, peak concentrations or weighted concentrations as a component for determining plant exposure/responses to ozone. A number of studies suggest that ozone flux (the rate at which plant surfaces absorb ozone) is the parameter, rather than ambient air concentrations, in determining plant exposure/responses. Understanding the relationship of atmospheric flux to ozone uptake is critical in determining plant response.

Plant response is determined by the amount of ozone taken up from the atmosphere by the canopies of individual plants within their respective agronomic, forest(s) or natural ecosystem setting. Ozone in the ambient air does not impair plant processes, only the ozone that diffuses

into the plants can elicit a response. The primary sites of ozone uptake are the leaf stomata. Uptake is controlled by stomatal conductance which varies as a function of the stomatal opening. Stomatal opening is controlled by the guard cells which are affected by a variety of environmental and internal factors including light, humidity, CO_2 concentration, plant water status and air pollutants. Understanding of the process of stomatal conductance is of importance in determining the amount of ozone that enters leaves as well as the subsequent plant responses.

Movement of ozone into the leaf cells involves both a gas and a liquid phase. Ozone in the gas phase must diffuse through the stomata (stomatal conductance) into the airspaces within the leaves and dissolve in the water coating the cell walls. An effect (response) will occur if a sufficient amount of ozone or its reaction products diffuse through or react with the cell membrane and reach sensitive sites within the cell. The uptake and movement of ozone to the sensitive cellular sites are subject to various physiological and biochemical controls. It has generally been accepted that ozone injury will not occur if the plant is able to (1) detoxify or metabolize ozone or its reaction products; or (2) repair or compensate for the impacts resulting from ozone uptake. The initial reactions of ozone with cellular constituents is not known. Determining the amount of ozone that actually enters the plant and what happens once it enters the air space within the leaf and how it causes an effect continues to be a puzzle.

The processes of detoxification and compensation also are not well understood. Physiological effects of ozone uptake are manifest in two ways: (1) reduced net photosynthesis and (2) increased leaf senescence. Both of these physiological effects decrease the capacity of plants to form carbohydrates. Plants not under stress allocate carbon compounds to leaves, stems and roots. A decrease in carbohydrate production alters the amount available for allocation to plant maintenance, injury repair, growth and reproduction. Root growth and the development of an association with mycorrhizal fungi are especially susceptible to reduced carbohydrate availability.

Plant exposure/responses are modified by various biological, physical, and chemical factors. Genetic composition (sensitivity or susceptibility), developmental stage (age and size) of the plant, cultivar (selection of crop or ornamental plant variety for ozone tolerance), site or habitat relationship, diversity within the canopy and location (overstory or understory)of the plant in the forest canopy, the influence of soil and water, and competition among native plants, especially those growing in a forest or grassland.

Human existence on this planet depends on the life-support services ecosystems provide. Human health is intimately associated with ecosystem functions. Ecosystems are essential for human life as we know it today. Ecosystems services include purification of air and water, mitigation of floods, soil fertility, generation and renewal of soil, translocation of nutrients, detoxification and decomposition of wastes, pollination of crops and natural vegetation, dispersal of seeds, and maintenance of biodiversity (variety of life at all levels of organization), from which humanity has derived key elements of its agricultural, medicinal and industrial enterprises.

Concern has risen in recent years regarding the consequences of changing the biological diversity of ecosystems. These concerns arise because there are few ecosystems on planet earth today that are not influenced by human activities. Human activities are creating disturbances that are altering the complexity and stability of ecosystems and are producing changes in biodiversity (structure and abundance of species), and functioning (energy flow, and nutrient cycling). Changes in biodiversity are producing harmful ecological, social, and economic consequences and an imbalance between supply and demand for ecosystems goods and services that could ultimately threaten human existence.

Ecosystem stress begins with the responses of sensitive individuals within a population. Ecosystem response to stress, however, depends on the impact the response of the sensitive species has on the species population. Growth characteristics arising from disturbance, changes in resource availability, or an otherwise changing environment, influence changes in community composition. Individual organisms within a population, based on their genetic constitution (genotype), stage of growth at time of exposure, and the microhabitats in which they are growing, vary in their ability to withstand the stress of environmental changes determines the response of the population. Responses, both structural and functional, must be propagated from the individual to the population and then to the more complex levels of community interaction to alter biodiversity and produce observable changes in an ecosystem.

Intense competition among plants for light, water, nutrients and space, along with recurrent natural climatic (temperature) and biological (herbivory, disease or pathogen) stresses, can alter the species composition of communities by eliminating those individuals sensitive to specific stresses, a common response in communities under stress. Those organisms able to cope with the stresses survive and reproduce. Competition among the different species in a community results in succession (community change over time) and ultimately produces ecosystems

composed of populations of plant species that have the capability to tolerate the stresses. Productivity, biomass, community height, and structural complexity increase during succession in unpolluted atmospheres. Severe stresses, on the other hand, divert energy from growth and reproduction to maintenance, and return succession to an earlier less complex stage. Ecosystems are subject to natural periodic stresses, such as drought, flooding, fire, and attacks by biotic pathogens (e.g., fungi and insects). When these natural disturbances are extremely severe, ecosystems of great complexity can be rapidly returned to an earlier successional stage of simpler structure with few or no symbiotic interactions. Perturbation of ecosystems by natural stresses are seldom more than a temporary setback, and recovery is generally rapid. Air pollution stresses, such as those caused by exposure to ozone, are superimposed on the naturally occurring stresses, on the other hand, are debilitating. Stressed ecosystems do not readily recover, but may be further degraded. Severe stresses which return succession to an earlier stage, reduce ecosystem structure and function. The plant processes of photosynthesis, carbon allocation and transformation, mycorrhizae formation, and nutrient uptake, that are directly related to energy flow and nutrient cycling are disrupted, food chains are shortened and the total nutrient inventory reduced. Areas denuded of vegetation can lead to nutrient leaching and runoff into aquatic ecosystems. Air pollutants by altering ecosystem structure and functioning and can affect the ecosystem services beneficial to society. Possible effects of air pollutants on ecosystems have been categorized as follows:

(1) accumulation of pollutants in the plant and other ecosystem components (such as soil and surface-and ground-water),
(2) damage to consumers (both human and animal) as a result of pollutant accumulation,
(3) changes in species diversity due to shifts in competition,
(4) disruption of biogeochemical cycles,
(5) disruption of stability and reduction in the ability of self-regulation,
(6) breakdown of stands and associations, and
(7) expanses of denuded zones.

The San Bernardino Forest studies have shown that stresses resulting from ozone exposures can alter the structure and functioning of an ecosystem. Changes in biodiversity occurred when the

sensitive canopy trees, ponderosa and Jeffrey Pine, were no longer able to compete effectively for essential nutrients, water, light and space. The altered competitive conditions in the plant community permitted the enhanced growth of more tolerant species and decreased biodiversity. The resulting changes in the functions of other ecosystem components directly or indirectly affected the processes of energy flow, mineral nutrient cycling, and water movement and lead to changes in community patterns. In addition, changes in available energy influenced biotic interactions associated with predator, pathogens, and the formation of mycorrhizae that play an import role in nutrient uptake. Because ozone has the potential to alter ecosystem structure and function in ways that may reduce their ability to meet societal needs, there is a need to know whether continuing ozone exposures are altering the plant composition, biodiversity, and function of additional ecosystems within the United States where plant and animal species are currently being exposed, and if so, to what extent these changes are affecting the ecosystem services important to human life.

Human society needs to be reconnected to the biologically diverse ecosystems and the natural world of which they are a part. There is a need to understand that biodiversity encompasses all levels of biological organization, including populations, individuals, species and ecosystems. Populations, geographical entities within a species of organisms, usually distinguished ecologically or genetically, are essential to the conservation of species diversity. Their number and size influence the probability of the existence entire species. The number, biodiversity, structure and functions of ecosystem populations, provide ecosystem benefits of both monetary and intrinsic value.

Attempts have been made to value biodiversity and the world's ecosystem services and natural capita and estimate economic and environmental benefits for services contributed from all biota (biodiversity), including their genes. Constanza et al. (1997) have estimated the total value of ecosystem services by biome for the entire biosphere. Ecosystems provide at least US$33 trillion worth of services annually. Constanza et al (1997) state that it may never be possible to make a precise estimate of the services provided by ecosystems. The above estimates, however, indicate the relative importance of ecosystem services.

Heal, however, feels that "Economics cannot estimate the importance of natural environments to society: only biology can do that" (Heal, 2000). The role of economics is to help design institutions that will provide incentives to the public and policy-makers for the

conservation of important natural systems and for mediating human impacts on the biologically diverse ecosystems and the biosphere so that they are sustainable (Heal, 2000). The establishment of ecological goals involves a close linkage between scientists and decision makers, in which science informs decision makers and the public by characterizing the ecological conditions that are achievable under particular management regimes. Decision makers then can make choices that reflect societal values, including issues of economics, politics and culture. For management to achieve their goals—the general public, scientific community, resource managers, and decision makers need to be routinely apprised of the condition or integrity of ecosystems in order that ecological goals may be established.

3.2 RESEARCH NEEDS AND RECOMMENDATIONS

Uncertainties in the data bases precluded EPA from setting a secondary NAAQS standard different from the primary NAAQS. The foregoing text listed Exposure Dynamics, Plant Response/Mode of Action, Ecosystems, and Economic Assessment as the four areas where research was needed to increase understanding of ozone effects on vegetation and ecosystems and to remove uncertainties and assist EPA in developing a secondary NAAQS for ozone that will protect vegetation. Further, the text discusses the importance, present state of knowledge of these areas and the areas where knowledge gaps exist.

Research to fulfill the above needs requires the coupling of ambient ozone concentrations at some height above the vegetation canopy to the micrometeorological conditions that facilitate ozone transfer to the canopy as well as an understanding of the physiological processes within plants that promote uptake and movement of ozone or its derivatives into the cells and the subsequent biochemical responses. Additional research needs should center on gaining a better understanding of the local site (habitat) and edaphic factors which may influence ozone exposures and uptake across local sites and larger regions, as well. Such information will aid in determining broad scale effects on the productivity and growth of crops, forests, wetlands, and native plants and impacts on ecosystem services within diverse regional scale ecosystems. Specific ecologically-related research needs are identified and discussed below.

1. Exposure: Determine the relationship between rural and urban ozone concentrations to exposures of natural vegetation, forest ecosystem, crop, and ornamental urban plants.

1a. Characterize variability in ozone exposure concentrations and duration on different scales.

Examine temporal (diurnal, frequency, duration, seasonal), spatial (rural, urban, landscape, regional), vertical (understory, canopy, vegetational) and altitudinal scales. Determine the time (exposure period) when sensitivity (susceptibility) is greatest i.e., resistance in different plants is lowest. Determine how the rate of uptake, exposure duration or exposure to low concentrations prior to "peaks" on affect plant response

1b. Quantify ozone exposure concentrations for rural areas where no monitors presently exist.

Develop monitoring networks using analytical monitors or passive monitors and modeling methodology to quantify exposures on a landscape, regional or national basis. Evaluate and compare results from passive and analytical monitors. Evaluate the use of the GIS technique for predicting exposures in remote areas where at present no monitors exist and for evaluating risk to vegetation. Develop and carry out modeling and spatial extrapolations to predict ozone exposures.

1c. Determine the co-occurrence of ozone exposure concentrations and nitrogen deposition in forested areas of the United States where both are most likely or known to occur.

Ozone exposure and nitrogen deposition stress trees both above and below ground.

2. Improve understanding of the exposure/response of individual plant species.

2a. Improve understanding of the relationships between ambient ozone concentrations and ozone flux to plant surfaces.

The timing of an exposure is critical in plant response. Exposure at the time the plant is most sensitive produces the greatest effect. Ozone must enter the plant to produce an effect. Improve understanding of the relationships between ambient ozone concentrations (peaks or mid-level) and ozone flux (rate at which plant surfaces absorb ozone)), stomatal conductance, and ozone uptake. Determine the role of ozone flux in "peak", "mid-level" and variable exposures in

and determine which exposure has the greater role in cumulative effects. Ozone fluxes typically vary though out the day. Stomatal conductances vary with cultivar, time of day and plant phenology. Determine the time of day plant sensitivity (stomatal conductance) is greatest and the factors (e.g., frequency, duration, temporal pattern of exposure and size) that influence it and its relationship to plant response. Determine the accuracy with which data from open-top chamber studies can be extrapolated to field exposures.

2b. Improve understanding of the biochemical and molecular basis for photosynthetic impairment and decreased carbohydrate allocation, plant growth and reproduction.

Impairment of photosynthesis impacts all other plant processes. Growth and seed formation depend not only on the rate of photosynthesis and uptake of water and nutrients, but also on the allocation of carbohydrates. Decrease in plant vigor, ability to compensate for injury and susceptibility to insect pest and fungal pathogens and allocation of carbohydrates to the roots all are related to photosynthetic impairment and decreased carbohydrate allocation. Improve understanding of how the degree to which plant resources are used for injury and repair alters patterns of carbohydrate allocation to the roots and for other plant processes, especially the role of genetics and age (phenology) in plant defense/tolerance and response. Improve understanding of the relationship between ozone exposure and insect pest/fungal pathogen interaction.

2c. Determine the relationship between visible leaf injury and injury at the more integrative levels of organ physiology (e.g., leaf cell, whole leaf, twig/branch, root, whole plant).

Visible leaf injury symptoms resulting from ozone exposures indicate that physiological changes are taking place at the cellular level. Scale responses from the molecular to the mature plant level. Investigate the defense (tolerance, detoxification, compensation) mechanisms (processes) that influence plant responses to ozone uptake and determine the transfer of responses to higher levels of organ physiology. The role of predisposition in influencing plant response varies from species to species and with environmental conditions. It is not understood well enough to permit a weighting function in characterizing plant exposures. Determine how the altered used of the carbohydrate budget influences plant response to subsequent exposures.

3. Ecosystems: Response of an individual plant species in an ecosystem.

3a. Understand how to extrapolate and compare effects of single season ozone exposure/responses (e.g, delayed responses or memory) with the effects of cumulative, multiple- year exposure/responses in seedlings and mature trees.

Competition for space, light, water and nutrients can impair growth and alter the biodiversity (vertical stratification of a population). Develop understanding of how O_3 exposures/response impairs the ability of sensitivity individual trees in a stand or population to compete for resources. Improve understanding of the cumulative physiological responses of trees to short-term and long-term O_3 exposures and the carry-over effects.

3b. Understand the importance of canopy structure and (habitat location or site, soil-moisture content, and microclimate) in ozone and tree response.

Improve understanding of the relationship between ozone exposures, crown injury symptoms, reduced photosynthesis and growth inhibition. Determine how the habitat or site, soil- moisture and microclimate influence plant response. Determine how the vertical stratigraphic location in a stand influences herbaceous plant, shrub or tree response to ozone exposures.

3c. Understand the importance of canopy structure and habitat (location or site, soil moisture content and microclimate) in O_3 uptake and tree response.

The sensitivity of various tree species within a forest, the canopy structure and habitat (location or site, soil moisture content and microclimate) can determine ozone uptake and tree response.

3d. Improve understanding of the relationship between ozone exposures, crown injury symptoms, reduced photosynthesis and growth inhibition.

Improve understanding of the affects of ozone exposure on annual, perennial and woody understory plant species and how the vertical stratification of individual species in a population, stand or community affects this response.

3e. Develop methodology to determine tree health.

For example, physiological changes such as altered carbohydrate allocation within trees can affect growth and the ability to compete for light, water, space and nutrients. Studies indicate that low levels of ambient ozone can significantly reduce growth of mature loblolly pine trees. Patterns of stem expansion and contraction using serial measurements with sensitive dendrometer band systems indicated ozone interaction with moisture stress and temperature inhibited the growth of mature trees growing in a forest. Determine whether this technique can be used to determine ozone growth inhibition in mature trees of other species.

4. Ecosystems: Effects on biodiversity, ecosystem processes and services.

4a. Understand how ozone exposures alter ecosystem structure and changes the role of key plant species and functional groups.

Changes in structure impact the critical processes of energy (carbon), water flow and resource availability (nutrient cycling) and ecosystem productivity. Species composition of plant functional groups (groups of species which, based on physiology, morphology, life history or other traits, control an ecosystem process) can have a greater affect on ecosystem processes than does the number of species in a functional group. Determine the key functional groups in a forest being exposed to injurious ozone concentrations. Determine how or whether the stresses resulting from the exposures alters species composition (biodiversity) of these functional groups and affects resource availability (nutrient cycling) and ecosystem productivity. Identify the changes in species abundance that are most likely to affect ecosystem processes and ultimately ecosystem productivity and services.

4b. Understand the impact of early needle or leaf senescence, altered successional patterns of leaf microflora on plant foliage and changes in litter decomposition patterns on mineral nutrient cycling, particularly nitrogen.

Ozone exposures can result in early needle or leaf senescence and alter succession of the microflora inhabiting leaves/needles. Changes litter quality, and decomposition rate and affect soil nitrogen availability and impact the below-ground food webs.

4c. Improve understanding of how ozone exposures that alter above-ground biodiversity of species impact below-ground diversity (altered mycorrhizal diversity and food webs) and the below-ground processes of nutrient cycling and ecosystem functioning.

The mutualistic relationship between plant roots, fungi and microbes is critical for the growth of the organisms involved. Mycorrhizal fungal diversity, especially arbuscular mycorrhizal fungi (AMF) is associated with above-ground plant biodiversity, ecosystem variability and productivity. Develop an understanding of the of the interrelationship between the effects of chronic nitrogen additions to the soil on mycorrhizal associations, nitrogen uptake, other soil processes and ozone exposure/responses of trees and other above-ground plant growth and ecosystem biodiversity and productivity.

5. Assessments:

5a. Identify the ecosystem services and products most impacted by ozone exposures.

Ecological risk involves the loss of biodiversity and its direct impact on ecosystem services and the products that benefit human society. Determine the impact to society of losses in biodiversity and ecosystem services, including indirect impacts on aquatic or terrestrial animal species of ozone-induced changes in plant biodiversity and shifts in wildlife habitat conditions.

5b. Develop updated economic analyses of ecological productivity and ecosystems services changed by ozone exposures.

Develop economic techniques to measure how changes in ecosystems biodiversity impact the value of ecosystem productivity and services. Develop an understanding of the relationship between ozone exposure/responses and altered forest biodiversity (altered tree and understory growth), decreased forest productivity, altered watershed function and the economic impact of the reduction in ecosystem services. Develop economic incentives for their preservation. Determine the economic costs of the impact on the urban and ornamental trees and shrubs of ozone exposures.

5c. Develop economic incentives in support of legislation to preserve ecosystem biodiversity and to improve crop protection.

Develop economic incentives for making the preservation of forest biodiversity of value. In certain regions of the United States crop loss related to ozone exposures is not of concern to farmers and growers because they have insurance. Develop economic incentives making reducing ozone exposures of greater benefit than the cost of crop insurance.

3.3 RESEARCH PRIORITIES

The lack of information necessary for determining the impact of ozone at the ecosystem level and for supporting a secondary NAAQS begins at the level of the individual plant and continues through the population and to the community and ecosystem level. The greatest need is for information at the ecosystem level. In the introduction to this section (3.1), it was pointed out that humans could not exist on this planet without ecosystem products and services. Anthropogenic stresses are causing the loss of biodiversity and altering the energy flow and nutrient cycling necessary for proper ecosystem functioning. Environmental stresses that are the result of human activities are irreversible. For this reason, a secondary NAAQS for ozone that will protect ecosystems and prevent their breakdown, is of the greatest priority. Therefore, there is a need for studies characterizing the impact of ozone exposures on biodiversity in forest ecosystems in both Eastern and Western forest ecosystems where ozone concentrations are high, but also in other areas where high ozone levels may be impacting ecosystems.

Whether changes in biodiversity have occurred as the result of ozone exposures can be determined only if there is data from which to establish a baseline. Except for the Los Angeles Basin in southern California, information concerning the long-term responses of ecosystems to ozone exposures is lacking. Ozone exposures in the Sierra Nevada in California and in the Southeast, specifically the Smoky Mountains National Park and the Appalachians have been increasing. The data in the Southeast dealing with the response of various ecosystem components is scattered both over time and region. However, a number of studies have outlined the main tendencies in the etiology of ecosystem breakdown (Rapport and Whitford, 1999). Assessment of the current status of the forest ecosystems in both the east and the west using the data currently available and making extrapolations based on the information provided in the

studies of the etiology of ecosystems breakdown as well as using data from the many published studies, some of which are cited above, that detail the changes in biodiversity and ecosystem services that result from anthropogenic ecosystem perturbations could provide guidelines for determining how ecosystems are responding to the major stress of ozone exposure.

Data to supplement the information concerning ecosystem response to the ozone stress cited in the above paragraph requires an integrative approach. Information from at least three levels of biological interaction are needed: (1) individual plant response, (2) response of population, and (3) the biological community composed of populations of many different species. The impact of the environment on the susceptible plants at each level as they interact with each other determines the response of the ecosystem. It also is necessary to improve and update the economic assessments of ecosystem effects. Detailing the economic importance to society of ecosystem products and services and developing economic incentives for their preservation would provide an important basis and enhance the need for a secondary NAQQS for ozone.

Thus, to understand long-term ecosystem effects of ozone there is a need for information in the major categories in this document. Listed in priority order these are: (1) Ecosystem Responses; (2) Assessments; (3) Monitoring; (4) Individual Plant Responses; and (5) Economic Impacts.

CHAPTER 4: SUMMARY OVERVIEW OF KEY OZONE RESEARCH NEEDS AND PRIORITIES

4.1 HEALTH-RELATED OZONE RESEARCH NEEDS

Key health-related ozone research needs derived from the workshop discussions noted earlier and refined by EPA staff (as discussed above) are summarized below. There are seven numbered needs in all, each with several lettered sub-items. The order of research needs presented reflects some, but only some, degree of prioritization. For example, available evidence suggests that the characterization of health effects of long-term ambient ozone exposure is a more pressing need than further characterization of short-term effects. Thus, assessment of long-term effects is placed before assessment of short-term effects. At the same time, it is emphasized that the order of numbered needs is intended more to reflect a reasonable conceptual flow than to suggest sequential prioritization. For example, needs related to ambient ozone exposure are placed before those related to health outcomes because, analytically speaking, exposure variables are independent variables whereas outcome variables are dependent variables. This order should not be taken to imply that exposure-related needs are more important than health outcome-related needs. Accomplishment of both is vital to achieve sufficient understanding of ambient ozone health effects. Similarly, in research needs related to characterization of health effects of long-term and short-term ozone exposure (research needs 2 and 3), experimental studies are listed before epidemiologic studies. This should not be taken to imply that experimental studies are more important than epidemiologic studies. On balance, each of the seven numbered research needs should be considered to have high priority.

There are several lettered items within each numbered research need. These items are assigned priorities according to a three-level scale. Highest priority (priority 1) is assigned to areas in which there is reason to suspect that further research would document a substantial public health burden of ambient ozone exposure, and in which there remains substantial scientific uncertainty. For example, priority 1 is assigned to two of three items under Research Need 2, "Improve understanding of health effects of long-term ozone exposure." Priority 1 is also assigned to items that pertain to improving characterization of population exposure to ambient ozone, to improving interspecies extrapolation, advancing understanding of single-pollutant effects relative to multi-pollutant effects, and characterizing population health benefits

of reduction of exposure to ambient ozone and other air pollutants. Priority 2 is assigned to areas in which further research would clearly advance understanding of ozone health effects, but which have somewhat less direct relevance to the ozone standard-setting process than do Priority 1 areas. Priority 3 is assigned to areas in which future research is judged to have less probability of ultimate success than research in priority 1 and 2 areas. Priority 3 is also assigned to areas in which past research efforts have been less informative to the standard-setting process than originally anticipated.

This document does not specifically address research needs related to economic impact of ozone-related health risks, because cost is not to be considered in setting primary NAAQS. At the same time, accomplishment of the research needs identified here would improve health-related inputs for economic valuation and cost-benefit evaluation efforts.

1. Improve understanding of human exposures to ambient ozone and to related, potentially harmful air pollutants.

1a. Gather population-based information on total human ozone exposure, sufficient to evaluate current and future ozone exposure models (Priority 1).

1b. Gather information needed to improve inputs to current and future population-based ozone exposure models (Priority 1).

1c. Improve understanding of atmospheric chemistry involving ozone, as needed to improve understanding of human exposure to ozone, particulate matter, and other potentially harmful air pollutants at the community level (Priority 2).

1d. Explore the utility of applying emissions-based ozone air quality modeling methods (currently used at the regional scale for attainment/compliance purposes) to the neighborhood scale, in order to provide supplemental assessment of human exposure to ambient ozone (Priority 3).

2. Improve understanding of health effects of long-term ozone exposure.

2a. Experimental studies of long-term ozone exposure (Priority 1).
2b. Epidemiologic studies of long-term ozone exposure (Priority 1).
2c. As feasible, develop and validate biomarkers of subchronic and chronic ozone exposure and effects in experimental and epidemiologic studies (Priority 2).

3. Improve understanding of health effects of short-term ozone exposure.

3a. Experimental studies of short-term ozone exposure (Priority 2).
3b. Epidemiologic studies of short-term ozone exposure (Priority 1).
3c. Develop and validate biomarkers of short-term ozone exposure and effects in experimental and epidemiologic studies (Priority 3).

4. Improve understanding of ozone dosimetry and augment interspecies extrapolation of ozone effects.

4a. Among different species, further characterize and compare inherent sensitivity to ozone, and ozone dosimetry in different regions of the respiratory tract (Priority 1).
4b. Characterize ozone mass transfer coefficients in different regions of the respiratory tract (Priority 1).
4c. Improve understanding of chemical reactions of ozone in the respiratory tract, especially in the lung lining fluids. Ascertain short-term and long-term biological processes triggered and influenced by ozone and its reaction products (Priority 2).

5. Identify subpopulations susceptible to ambient ozone and characterize health effects of ozone and co-pollutants in these subpopulations.

5a. Experimental studies of ozone susceptibility (Priority 2).
5b. Epidemiologic studies of ozone susceptibility (Priority 1).

6. Determine biological mechanisms of injury induced by ozone alone, and by ozone in combination with co-pollutants.

6a. Further characterize the nature and time course of ozone-induced cellular and tissue injury (Priority 1).
6b. Further characterize the nature and time course of sequelae of ozone-induced injury (Priority 1).

7. Characterize health benefits of reduction of exposure to ambient ozone and other air pollutants.

7a. Conduct experimental studies designed to assess health benefits of reduction of exposure to ozone and other environmental pollutants (Priority 2).
7b. When feasible, conduct epidemiologic studies and population surveillance in locations that experience reduction in ambient ozone concentrations (Priority 1).

4.2 ECOLOGICAL RESEARCH NEEDS FOR OZONE

Ecological risk assessment is a complex process. Comprehensive analysis of the impact on ecosystems necessitates the integration of information from at least four interdependent areas of

research. These are: exposure dynamics, plant response, ecosystem response, and assessment of economic and ecosystem (product/services) impacts. These four areas are critical for obtaining information to develop a secondary standard for ozone. Each area has its own priorities. Real time data for characterizing actual ozone exposures across broad regional expanses of rural, agricultural, and remote forested areas is lacking. Monitoring to determine ambient ozone concentrations encountered in urban, rural farm/forest areas, exposure patterns (episodes), concentrations vs flux, relationship between chamber and field exposure data, and plant uptake are needed. Plant response and mode of ozone action begins with response of individual plants. Individual plant response is a culmination of a sequence of physical, biochemical and physiological events. There are knowledge gaps in each step of the sequence. The events occurring in plant exposure-response are so numerous, and so closely integrated, that it is difficult to designate a single top priority.

Probably the greatest overall need is to improve understanding of the cellular, biochemical, and physiological mechanisms that occur once ozone has entered into the air spaces though the stomata and dissolved in the water on the call walls. Further understanding of these events would improve understanding of the molecular and biochemical bases for photosynthetic impairment and decreased allocation of the carbohydrates necessary for plant growth and reproduction. Also, it would improve understanding of individual plant sensitivity, site/habitat influences and pest, disease, and abiotic stress interactions. This is not a priority that can be accomplished in a short period of time, as it has not been solved during all of the years of air pollution research. (However, understanding of the steps occurring after the initial entry of ozone has improved to some degree).

A second priority is determining which parameter, ambient ozone concentration or ozone flux relates best to exposures. Also, there is a need to understand the role of “peak”, “mid-level” and variable concentrations in producing ozone effects. Determining ozone impact on ecosystems is the most difficult of all because there are many and varied plant species in an ecosystem, and because these species engage in complex interactions with each other and with the overall environment.

There is a need for increased understanding of the exposure-response relationships of sensitive individual native plant species and forest trees to ozone, under ambient conditions, and

the characterization of the impact of exposures on interspecies competition on both above and below ground organismal interactions.

The impact of ozone on the various living components of an ecosystem results in economic impacts on products (biomass and yield of crops, forests, etc.) and ecosystem services. Understanding ecosystem responses will aid in managing ozone impacts and in determining the benefits that can be derived from control of ozone exposures. Studies to date have concentrated on vegetation response, especially response of individual plants to ozone exposures and the subsequent events that occur because plants are the most visible and therefore easiest to study.

Research needs for each area are outlined below and discussed in greater detail in Chapter 3, Section 3-1.

1. Exposure: Determine the relationship between rural and urban ozone concentrations to exposures of natural vegetation, forest ecosystem, crop, and ornamental urban plants.

1a. Characterize variability in ozone exposure concentrations and duration on different scales (Priority 1).

1b. Quantify ozone exposure concentrations for rural sites where no monitors presently exist (Priority 2).

1c. Determine the co-occurrence of ozone exposure concentrations and nitrogen deposition in forested areas of the United States where both are most likely or known to occur (Priority 3).

2. Improve understanding of exposure/responses of individual plant species.

2a. Improve understanding of the relationships between ambient ozone concentrations (peaks and mid-level) and ozone flux (rate at which plant surfaces absorb ozone), stomatal conductance and ozone uptake. Determine the time of day and the factors (e.g., frequency, duration, temporal pattern of exposure and size) that influencing plant response. Determine the accuracy with which data from open-top chamber studies can be extrapolated to field exposures (Priority 1)

2b. Improve understanding of the biochemical and molecular basis for photosynthetic impairment and decreased carbohydrate allocation and alteration of other physiological processes, on plant growth and reproduction. Improve understanding of the relationship between reduced carbohydrate allocation and increased susceptibility to insect pests and fungal pathogens (Priority 2).

2c. Determine the relationship between visible leaf injury and injury at the more integrative levels of organ physiology (e.g., leaf cell, whole leaf, twig/branch, root, whole plant). Scale responses from the molecular to the mature plant level. Improve understanding of the role of predisposition in plant sensitivity (Priority 3).

3. Ecosystems: Response of individual plant species in an ecosystem.

3a. Improve understanding of how to extrapolate and compare individual seedling/sapling responses to zone with the response of mature trees of varying age (Priority 1).

3b. Improve understanding of how ozone exposure/responses impair the ability of sensitive individual trees in a stand or population to compete for resources of space, light water, and nutrients. Develop methodology to determine tree health (Priority 2).

3c. Improve understanding of the relationship between ozone exposures, crown injury symptoms, reduced photosynthesis and growth inhibition. Understand the importance of canopy structure and habitat in ozone uptake and tree response (Priority 3).

4. Ecosystems: Affects on biodiversity and on ecosystem processes and services.

4a. Understand how ozone exposures alter ecosystem structure and change the role of key plant species and functional groups. Identify the changes in species abundance that are most likely to affect ecosystem processes and ultimately ecosystem productivity and services (Priority 1).

4b. Understand the impact of changes in microorganismal leaf succession affect, decomposition patterns mineral nutrient cycling, particularly nitrogen (Priority 2).

4c. Improve understanding of the interrelationships between ozone exposures/response, altered above- and below-ground diversity and below-ground processes (Priority 3).

5. Assessments: Improve assessments of economic impact of ozone exposure on ecosystem services.

5a. Identify ecosystem services most impacted by ozone exposures (Priority 1).

5b. Develop updated economic analyses of ecological productivity and services changed by ozone exposures (Priority 2).

5c. Develop economic incentives supporting legislation for preserving ecosystem biodiversity and to make reduction of ozone levels a greater value than crop insurance (Priority 3).

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APPENDIX I-A

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Participants' names are organized by disciplinary discussion group.

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APPENDIX II-A

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